

REMARKS

Claims 1-21 are pending in the above-referenced application, and all of the claims are rejected.

Rejection under 35 U.S.C. 103(a)

The Examiner rejects claims 1-3, 5-7, 9-10, 12-14, and 17-21 under 35 U.S.C. 103(a) as unpatentable over Novak *et al.* in view of Delisle. According to the Examiner, it would have been obvious to exchange the glucose carbon source taught by Novak *et al.* for the sucrose carbon source taught by Delisle. Applicants previously explained that the prior art methods do not result in production levels as great as the instant invention. Applicants respectfully submit that the Examiner does not give this argument its proper weight. The law is clear that unexpectedly superior results are sufficient to rebut a *prima facie* case of obviousness.

The Examiner rejects claims 1-21 under 35 U.S.C. 103(a) as unpatentable over Qi *et al.* in view of DeVuyst *et al.* According to the Examiner, it would have been obvious to exchange the glucose carbon source taught by Qi *et al.* for the sucrose carbon source taught by DeVuyst *et al.* Just as described above, Applicants previously explained that the prior art methods do not result in production levels as great as the instant invention. Applicants respectfully submit that the Examiner once again does not give this argument its proper weight.

As the Examiner knows, in order to establish a proper *prima facie* case of obviousness, the Examiner must establish that there is a suggestion or motivation to modify the references or to combine the reference teachings; there must be a reasonable expectation of success; and the references or combination of references must teach or suggest all of the claim limitations (*see, e.g.,* MPEP § 2142). The teachings or suggestions to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cr. 1991)). The arguments advanced by the Examiner fail to meet all of these criteria. There simply is no suggestion or expectation of success within the references cited for changing the glucose carbon source of Novak *et al.* for a sucrose carbon source.

The patent law is also quite clear that even if, *assuming arguendo*, there was a proper

prima facie case of obviousness, secondary considerations may be used to rebut such a *prima facie* case. Among these secondary considerations are unexpectedly superior results. The methods of the prior art simply do not result in production levels as great as the instant invention as described in paragraph 10 of the specification. Therefore, even if, *assuming arguendo*, there were a proper *prima facie* case of obviousness, the present methods are rendered patentable because they produce unexpectedly superior production levels.

Key factors for mutacin I and III submerged production

Applicants herein further elaborate on the patentability of the instant invention. All of the following explanations are presented under oath by the Declarant Zenggo He, Ph.D. The following explanations will clarify that there was no motivation to substitute sucrose for glucose, that there was no reasonable expectation of success in producing mutacin I and III if sucrose was used since no mutacin I and III were produced using glucose, and that the production levels attained were unexpected.

Previously, four mutacins were found in the laboratory by different *Streptococcus mutans*. Mutacin I, II and III are lantibiotics whereas mutacin IV is not. Mutacin I and III have a stronger antimicrobial potency as compared with mutacin II and V.

Techniques for submerged production of mutacin II had been successfully worked out, by using media applying glucose as the carbon source. However, when the same conditions were used for mutacin I and III in submerged culture, no obvious production was observed. Thus before the invention, submerged production of mutacin I and III was not possible. The instant invention is directed to methods for successfully producing the same in a liquid culture. One of the key factors that allows producing mutacin I and III is the use of sucrose.

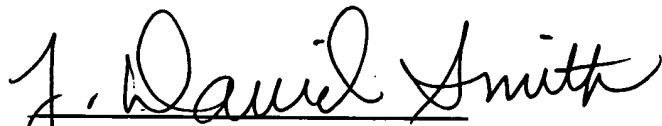
It is reported that one of the most crucial conditions for mutacin I and III is cell density. In solid culture, the producer cells form into bio-film based colonies. Thus, mutacin I and III can be produced in any media tested. However, in liquid culture, reaching a biofilm based high cell density is a huge challenge. This is clarified by the unexpected failure to produce mutacin I and III when media having glucose as the carbon source are used.

The presently claimed methods unexpectedly overcome this difficulty by using an OPM medium having sucrose as the carbon source. This medium allows exopolysaccharide production and enables the producer cells to aggregate together and form into pellets (*See*, Figure 1, submitted herewith). Thus, the present invention produces biofilm based high cell density (*See*, Figure 2, submitted herewith). As a result, an unexpectedly high yield of both mutacins I and III in submerged culture is attained. A cell pellet is unexpectedly never observed in a media having glucose as the carbon source (*See*, Figure 3, submitted herewith).

Conclusion

Applicants believe that the foregoing comments place the application in condition for allowance. Withdrawal of the rejections and objections is respectfully requested. If a discussion with the undersigned will be of assistance in resolving any remaining issues, the Examiner is invited to telephone the undersigned at (201) 487-5800, ext. 114, to effect a resolution.

Respectfully submitted,

A handwritten signature in black ink, reading "J. David Smith". The signature is written in a cursive, flowing style. The first letter "J" is large and loops around the first part of the name. The last name "Smith" is written in a similar cursive style.

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